

AMENDMENTS TO THE CLAIMS

1. (Currently amended): A method to isolate and characterize a membrane-bound receptor along with its microenvironment which method comprises

providing a solid support coupled to a ligand which specifically binds said receptor, wherein said ligand is a cognate binding agent other than a lectin;

treating said solid support with a sample comprising nucleated cells or organelles thereof comprising said membrane-bound receptors, and which cells or organelles have not been surface-treated,

wherein a complex is formed between said membrane-bound receptor and the ligand thus generating a ligand/receptor complex comprising the receptor and its microenvironment, wherein the microenvironment includes additional non-covalently associated cellular components, which complex is coupled to solid support through the ligand thus providing a complexed solid support;

separating the complexed solid support from the remainder of the sample;

subjecting the separated complexed solid support to a force sufficient to dissociate the receptor and its microenvironment from the membrane but insufficient to disrupt the ligand/receptor complex $[[;]]$, thus obtaining complexed solid support coupled to a ligand/receptor complex whereby the receptor retains its microenvironment but is separated from the membrane,

removing the ligand/receptor complex comprising the receptor and its microenvironment from the complexed solid support $[[,]]$; and

analyzing the microenvironment of the receptor, wherein the microenvironment is analyzed by chromatographic analysis or mass spectrometry.

whereby a membrane-bound receptor along with its microenvironment is isolated and characterized.

2-3. (Canceled)

4. (Original): The method of claim 1 wherein the cells are vertebrate cells.

5. (Original): The method of claim 4 wherein the cells are tumor cells or diseased cells.

6. (Previously presented): The method of claim 1 wherein the cells are hematopoietic cells, or cells from adipose, areolar, connective, elastic, epithelial, endothelial, neural, mucous or reticular tissues.
7. (Original): The method of claim 1 wherein the ligand is an antibody or an immunospecific portion thereof.
8. (Original): The method of claim 1 wherein the receptor comprises an HLA antigen.
9. (Original): The method of claim 1 wherein the receptor comprises a tumor associated antigen.
10. (Original): The method of claim 1 wherein the receptor is a cytokine receptor, a hormone receptor, an opioid receptor, or a steroid receptor.
11. (Original): The method of claim 1 wherein the force is achieved through extrusion.
12. (Original): The method of claim 1 wherein the force is achieved through vortexing or shaking.
13. (Original): The method of claim 1 wherein the force is achieved through sonication.
14. (Original): The method of claim 1 wherein the solid support comprises beads.
15. (Original): The method of claim 14 wherein said beads are polyacrylamide beads, polystyrene beads, Sephadex beads, or latex beads.
16. (Original): The method of claim 1 wherein the solid support is a multi-well plate.
17. (Previously presented): A method to isolate and characterize a membrane-bound receptor along with its microenvironment which method comprises

providing a solid support coupled to a ligand which specifically binds said receptor, wherein the ligand is coupled to the solid support through a linker containing a photocleavable portion;

treating said solid support with a sample comprising nucleated cells or organelles thereof comprising said membrane-bound receptors, and which cells or organelles have not been surface-treated,

wherein a complex is formed between said membrane-bound receptor and the ligand thus generating a ligand/receptor complex comprising the receptor and its microenvironment, wherein the microenvironment includes non-covalently associated cellular components, which complex is coupled to solid support through the ligand thus providing a complexed solid support;

separating the complexed solid support from the remainder of the sample;

subjecting the separated complexed solid support to a force sufficient to dissociate the receptor and its microenvironment from the membrane but insufficient to disrupt the ligand/receptor complex, thus obtaining complexed solid support coupled to a ligand/receptor complex whereby the receptor retains its microenvironment but is separated from the membrane;

removing the ligand/receptor complex comprising the receptor and its microenvironment from the complexed solid support by exposing the linker to light; and

analyzing the microenvironment of the receptor.

18. (Previously presented): The method of claim 1 wherein the ligand is coupled to solid support through a linker containing a portion cleavable by an enzyme and said removing is effected by exposing said linker to said enzyme.

19. (Canceled)

20. (Currently amended): A method to recover a multiplicity of receptors along with their microenvironments which method comprises:

providing a multiplicity of solid support portions each coupled to a different ligand, wherein said ligand is a cognate binding agent other than a lectin;

treating said multiplicity of solid support portions with a sample comprising nucleated cells that comprise at least two cell surface receptors, wherein said cells are not surface treated under

conditions wherein ligand/receptor complexes are formed between said ligands and receptors at said cell surfaces which complexes are coupled to said solid support portions through the ligands, thus providing complexed solid support portions;

removing the complexed solid support portions from the sample; and

subjecting the complexed solid support portions to forces sufficient to remove the receptors and their microenvironments, wherein the microenvironment includes additional non-covalently associated cellular components, from the surface of said cells but insufficient to disrupt the ligand/receptor complexes [,.] ;

removing the ligand/receptor complexes comprising the receptors and their microenvironments from the complexed solid support portions [,.] ; and

analyzing the respective microenvironments of at least two receptors, wherein the microenvironment is analyzed by chromatographic analysis or mass spectrometry,

whereby a membrane-bound receptor along with its microenvironment is isolated and characterized.

21. (Canceled)

22. (Original): The method of claim 20 which further includes identifying the receptors.

23. (Canceled)

24. (Original): The method of claim 22 which further includes organizing the identified receptors into a profile characteristic of the membrane sample.

25-26. (Canceled)

27. (Previously presented): The method of claim 20 wherein said ligands are monoclonal antibodies.

28. (Previously presented): A method to recover a multiplicity of receptors along with their microenvironments which method comprises:

providing a multiplicity of solid support portions each coupled to a different ligand, wherein the ligands are coupled to the solid support portions through linkers each containing a photocleavable site;

treating said multiplicity of solid support portions with a sample comprising nucleated cells that comprise at least two cell surface receptors, wherein said cells are not surface treated under conditions wherein ligand/receptor complexes are formed between said ligands and receptors at said cell surfaces which complexes are coupled to said solid support portions through the ligands, thus providing complexed solid support portions;

removing the complexed solid support portions from the sample; and

subjecting the complexed solid support portions to forces sufficient to remove the receptors and their microenvironments, wherein the microenvironment includes additional non-covalently associated cellular components, from the surface of said cells but insufficient to disrupt the ligand/receptor complexes;

removing the ligand/receptor complexes comprising the receptors and their microenvironments from the complexed solid support portions by exposing the linkers to light; and analyzing the respective microenvironments of at least two receptors.

29. (Previously presented): The method of claim 20 wherein the ligands are coupled to solid support portions through linkers each containing a site cleavable by an enzyme and said removing is effected by exposing said linkers to said enzyme.

30. (Previously presented): The method of claim 20 wherein the cells are vertebrate cells.

31. (Previously presented): The method of claim 30 wherein the cells are tumor cells or diseased cells.